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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/347,748	12/01/1994	KENNETH KAUSHANSKY	94-9C2	4530

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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/347,748	KAUSHANSKY, KENNETH	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 9-13,15-22 and 24-31 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 9-13, 15-22, 24-31 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 9-13, 15-22, 24-31 are pending and under consideration by the Examiner. The indicated allowability of claims 9-13, 15-22, 24-31 is withdrawn. Prosecution in this case is being reopened. An office action on the pending claims follows.

Claim rejections-35 USC § 112, first paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2a. Claims 9-13, 15-22, 24-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case sets forth a method for stimulating erythropoiesis by using a mouse thrombopoietin (TPO) of amino acid sequence set forth in SEQ ID NO:4 and therefore the written description is not commensurate in scope with the claims drawn to a method for stimulating erythropoiesis by using a mammalian thrombopoietin or species homologs of SEQ ID NO:4 which encompass porcine, equine, rodent, bovine and other mammalian TPO's.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of SEQ ID NO:4, the skilled artisan cannot envision the detailed structure of the vast species of TPO's encompassed by the claims and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid and protein itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids or proteins by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate

written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Support for the amino acid sequence set forth in SEQ ID NO:4 is provided in the specification on page 9, lines 20-24. However, no disclosure, beyond the mere mention of other species homologs is made in the specification (see page 9, lines 32-35). This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only a method for stimulating erythropoiesis by administering a mouse TPO of amino acid sequence set forth in SEQ ID NO:4 but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. As a result, it does not appear that the inventors were in possession of variants of mammalian TPO or species homologs thereof.

2b. Claims 9-13, 15-22, 24-31, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for stimulating erythropoiesis by using a mouse thrombopoietin (TPO) of amino acid sequence set forth in SEQ ID NO:4, does not reasonably provide enablement for a method for stimulating erythropoiesis by using all mammalian thrombopoietin (TPO) or a species homologue of the protein of amino acid sequence set forth in SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

With respect to claim 9 (for example), the specification is not enabling for "a species homolog" of the protein of amino acid sequence set forth in SEQ ID NO:4, since no reasonable

expectation of success and no working example of species homologs of the protein comprising the amino acid sequence shown in SEQ ID NO:4 have been provided in the specification.

The specification provides only sequence data to allow one to characterize the proteins of SEQ ID NO:2 or 4. Many distinct proteins may share the same activity, so that even if one were to determine a biological activity of the protein, say promotion of cell growth, many distinct proteins would have this activity (e.g. many different growth factors, interleukins, hormones, oncogenes). As a result, if one were to isolate a protein from a different species that had the same activity, one could not reasonably predict if the isolated protein was a species homologue of the original protein because one could not determine if the sequence difference between the original and isolate were due to species differences or to the proteins being non-homologous but sharing the same activity. Further, the specification provides insufficient guidance to allow one to obtain species homologues.

Additionally species homologues often display low sequence identity so that identification based solely on sequence similarity is impossible. Under such common circumstances, it is impossible to identify species homologues. For example in The Cytokine Facts Book (1994), Robin Callard and Andy Gearing. Academic Press Inc. San Diego, CA, the amino acid sequence of IL-2 (interleukin-2) from human compared to mouse differs by 16 amino acids in length (page 39, table) and share only about 60% identity (page 39, "Crossreactivity" section). Based solely on sequence, it would be clearly impossible for one skilled in the art to identify the mouse and human proteins as species homologues; however, when one is able to compare a known or putative activity (page 39, "Bioassays" section"), identity can be confirmed.

Furthermore, Reeck et al. (line 1-2) point out, ""Homology" has the precise meaning in biology of "having a common evolutionary origin,"...".

It is stated at the top of column 2 that:

A similarity, then, can become a fully documented, simple fact. On the other hand, a common evolutionary origin must usually remain a hypothesis, supported by a set of arguments that might include sequence or three-dimensional similarity. Not all similarity connotes homology but that can be easily overlooked if similarities are called homologies. Thus, in this third case, we can deceive ourselves into thinking we have proved something substantial (evolutionary homology) when, in actuality, we have merely established a simple fact (a similarity, mislabeled as homology). Homology among similar structures is a hypothesis that may be correct or mistaken, but a similarity itself is a fact, however, it is interpreted.

Reeck et al. provided emphasis to the above reasons for not being able to identify, if one is able to isolate candidates, species homologues as claimed because of the lack of guidance and information in the current specification.

Claim rejections-35 USC § 112, second paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3a. Claim 9-13, 15-22, 24-31 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9, 18, 28-31, are vague and indefinite because they recite "species homologs". The metes and bounds of this term are unclear. Does the term include rodent, porcine, equine, bovine homologs or some other species homologs?

Claims 18 and 28, lines 12-13, are unclear because it cannot be determined from the way the claim is written whether the erythropoietin is also administered. It is suggested that the claim be amended to recite in the preamble of the claim that TPO and erythropoietin are administered.

Claim 30, line 11, recites the limitation "thrombopoietin proteins". There is insufficient antecedent basis for this limitation in the claim.

Claims 10-13, 15-17, 19-22, 24-27, are rejected as vague and indefinite insofar as they depend on the above rejected claims for their limitations.

Conclusion

No claim is allowed.

Claims 9-13, 15-22, 24-31 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D., J.D.
Primary Examiner
Art Unit 1646
September 7, 2006